UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/687,051	10/12/00	BUECHLER	K	030691.0008.

HM22/0926

MICHAEL A. WHITTAKER
BROBECK, PHLEGER & HARRISON LLP
12390 EL CAMINO REAL
SAN DIEGO CA 92130

EXAMINER	
GABEL, G	
ART UNIT	**PAPER NUMBER**
1641	6

DATE MAILED: 09/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Applicati n No. 09/687,051	Applicant(s) BUECHLER ET AL.	
	Examiner Gailene R. Gabel	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *55-78* is/are pending in the application.

4a) Of the above claim(s) *55-68 and 75-78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *55-78* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II, claims 69-74, with traverse, in Paper No. 5 is acknowledged and has been entered. Claims 55-68 and 75-78 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Currently, claims 55-78 are pending. Claims 69-74 are under examination.

2. Applicant's traversal of the restriction requirement in Paper No. 5 is acknowledged. The traversal is on the grounds that no serious burden exists in examining all groups of invention.

This is not found persuasive because restriction requirements are set forth for reasons of patentable distinction between each independent invention so as to warrant separate classification and search. For example, the structural requirements for a "product" differ from the structural requirements for a "process of using" the product. Literature search for each product and method is distinct since the structural requirements of each invention are different. While searches would be expected to overlap, there is no reason to expect the searches to be coextensive.

The record set forth in the previous restriction requirement clearly indicated that the delineated inventions are in fact patentably distinct each from the other or independent from the other. The requirement is still deemed proper and is therefore made FINAL for reasons of record.

Currently, claims 69-74 are pending and under examination.

Oath/Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> It does not identify the post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation.

Abstract

4. Applicant is reminded of the proper language and format for an abstract of the disclosure. The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 250 words. It is important that the abstract not exceed 250 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The language should be clear and concise and should not repeat information given in the title.

Priority

5. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior applications in the first sentence of the specification (37 CFR 1.78) including the status of each application.

Information Disclosure Stat m nt

6. The Information Disclosure Statement (PTO-1449), filed January 22, 2001 in Paper No. 3 is acknowledged. References AC and AF were not considered because neither an English translation nor a statement of relevancy was provided therefor. Further, references AD, AG-AH, AM, AS, AV, AY, AZ, BC, BS, and BT were not considered because no copies have been provided therefore.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 69-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 72-74 have improper antecedent basis problems in reciting "A method according to claim ...".

Claim 69 is vague and indefinite in reciting "said antibody is insensitive with respect to each form of cardiac troponin I" because the term "insensitive" is a subjective term that lacks a comparative basis for defining its metes and bounds. As recited, it is unclear what Applicant intends to encompass by the term "insensitive" as used in the claim.

Claim 70 is vague and indefinite in reciting "said antibody is insensitive with respect to each form of cardiac troponin I" because the term "insensitive" is a subjective

term that lacks a comparative basis for defining its metes and bounds. As recited, it is unclear what Applicant intends to encompass by the term "insensitive" as used in the claim.

Claim 71 is vague and indefinite in reciting "provide an assay response that is insensitive with respect to each form of cardiac troponin I" because the term "insensitive" is a subjective term that lacks a comparative basis for defining its metes and bounds. As recited, it is unclear what Applicant intends to encompass by the term "insensitive" as used in the claim. Further, it is unclear what Applicant intends to encompass in reciting "assay response", i.e. binding affinity between elements in the assay.

Claim 74 is vague and indefinite in reciting "selecting two antibodies, each of which is insensitive with respect to each form of cardiac troponin I" because the term "insensitive" is a subjective term that lacks a comparative basis for defining its metes and bounds. As recited, it is unclear what Applicant intends to encompass by the term "insensitive" as used in the claim.

In as far as the term "insensitive", although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, if the term "insensitivity" refers to an antibody's inability to "recognize or distinguish between isoforms of troponin" by virtue of its "binding or affinity to each one of the isoforms within equivalent degrees", or otherwise lack of specificity towards a particular isoform, then such similar language can better effect clarity and definiteness in the recited claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

As stated in the specification at page 11, lines 21-22 "an insensitive antibody which is useful in an immunoassay does not distinguish one form or forms of troponin from another", in this case, cardiac troponin I, from here on cTnI forms". Further stated at page 6, lines 16-17, "an insensitive antibody is one that will tend to bind more than one form of troponin", in this case cTnI forms, i.e. free cTnI and complexed cTnI". Alternatively, a "sensitive antibody distinguishes one form or forms of cTnI from another form". By those definitions, Examiner interprets the claimed "insensitive antibody" as antibody that specifically binds cTnI, wherein the antibody does not differentially bind, or otherwise has reactivity towards all the recited cTnI forms including 1) free cTnI; 2) cTnI in a binary complex with troponin C (TnC), from here on cTnI/TnC complex; and 3) cTnI in a ternary complex with troponin T (TnT), from here on TnI/TnC/TnT complex; or wherein the antibody has equal affinity to all three forms of cTnI recited.

8. Claims 69-72 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Bodor et al. (Clinical Chemistry, 1992).

Bodor et al. develop monoclonal antibodies that bind human cTnI for use in troponin immunoassays. Bodor et al. specifically use purified cTnI in assessing

characterization of the monoclonal antibodies (see Abstract page 2204). The cardiac specificity of the purified mAbs was assessed using solid phase ELISA wherein each antibody was tested to observe for binding with cTnI (cTnI coated plates) and cTnI /TnC complex (TnC/TnI-coated plates). In mAb competitive studies using microplates coated with cTnI/TnC complex, Bodor et al. disclose that some mAbs are insensitive, i.e. bind and recognize different epitopes of cTnI, such as mAbs 3C5.10 and 1E11.3 which have reactivity towards free cTnI and enhanced reactivity towards cTnI/TnC complexes. Bodor et al. further found that 5 other mAbs, including mAbs 2B1.9, 7B11.4, 3D11.11, 1D12.6, and 2F6.6, are also insensitive with respect to each of the cTnI and cTnI/TnC forms, i.e. have reactivity to cTnI and cTnI/TnC complexes or independently bind both free and complexed cTnI (react with cTnI regardless of the presence of TnC). Bodor et al. also identify some mAbs as sensitive, i.e. specifically bind and recognize the same epitopes of cTnI, i.e. 5D4.1 mAb which binds and recognizes only specifically cTnI/TnC complexes (see page 2205 and 2207 column 2, Figure 1). In page 2206, column 1, Bodor et al. disclose the insensitive mAbs as being immobilized on a solid phase (microtiter plates) and the mAbs as being conjugated to a signal generating element (alkaline phosphatase labeled) in order to assess their suitability for use in assays (see page 2206, column 1). Finally, Bodor et al. teach that in ELISA of cTnI, use of mAbs allows greater reproducibility of reagents than polyclonal antibodies (see page 2212, column 2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 73 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bodor et al. (Clinical Chemistry, 1992).

Bodor et al. has been discussed supra. Bodor et al. differ in failing to disclose that the antibodies set forth provide a signal within about 20% equimolar amounts for each form of cTnI.

However, identifying and selecting mAbs or pAbs that can provide a signal within about 20% equimolar amounts, a result effective variable, can be achieved by routine optimization procedure. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the

prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Therefore, absent unexpected results, it would have been obvious for one of ordinary skill to have discovered the optimum workable value from the method disclosed by Bodor et al. by normal optimization procedures.

10. No claims are allowed.

Remarks

11. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Wicks et al. (US 5,756,682) disclose a polyclonal antibodies specific for cTnI used in conjunction with troponin subunit C as the other binding partner in a sandwich assay.

Isawa et al. (US 5,141,736) discloses the production of polydomas by fusing a hybridoma which produces an antibody with another hybridoma which produces an antibody against another target antigen (see column 6, lines 11-45). This fusion produces hybrid monoclonal antibodies which retain the ability to bind both target antigens (see column 7, line 55- column 8, line 29).

Buechler et al. (US 5,480,792) disclose methods for detecting the presence or amount of target ligand using antibodies which bind to the complex of ligand receptor and target ligand.

Larue et al. (Clinical Chemistry, 1993) disclose twenty five monoclonal antibodies which recognize only cTnI and 15 other mAbs which recognize both cTnI and skeletal TnI.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
September 19, 2001

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
09/24/01